

## **ATTACHMENT B**

### **Amendments to the Claims**

Please cancel claim 18 without prejudice or disclaimer.

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Withdrawn) A method for the non-invasive determination of the concentration of a substance (glucose) in blood of a subject, the method comprising the steps of:
  - (a) placing an electrical conducting probe against a skin surface of the subject, wherein the probe comprises a plurality of electrodes, each electrode comprising a spike, the spikes being laterally spaced apart from each other and being of sufficient length to penetrate the stratum corneum;
  - (b) passing an electrical current through the electrodes to obtain a value of impedance for the skin; and
  - (c) converting the impedance to said concentration.
2. (Withdrawn) A method according to claim 1, wherein each spike is at least 10  $\mu\text{m}$  in length.
3. (Withdrawn) The method of claim 1, wherein the probe comprises three said electrodes, the spikes of first and second of the electrodes being laterally spaced a first distance from each other, the spikes of the first and third electrodes being laterally spaced a second distance from each other, and wherein and step (b) includes

separately passing an electrical current between the first and second electrodes and the first and third electrodes to obtain first and second said values of skin impedance.

4. (Withdrawn) The method of claim 3, wherein the first and second distances are different from each other.

5. (Withdrawn) The method of claim 3, wherein the first distance is between about 0.1 mm and about 40 mm; or between about 0.1 mm and 30 mm; or between about 0.1 mm and 25 mm; or between about 0.1 mm and 20 mm; or between about 0.1 mm and 15 mm; or between about 0.2 mm and 10 mm; or between about 0.2 mm and 8 mm; or between about 0.2 mm and 5 mm; or between about 0.2 mm and 3 mm; or between about 0.2 mm and 2 mm; or between about 0.2 mm and 1.5 mm; or between about 0.2 mm and 1 mm; or between about 0.2 mm and 0.5 mm.

6. (Withdrawn) The method of claim 5, wherein the second distance is between about 1 mm and about 50 mm; or between about 1 mm and 40 mm; or between about 1 mm and 30 mm; or between about 1 mm and 25 mm; or between about 1 mm and 20 mm; or between about 1 mm and 15 mm; or between about 1 mm and 10 mm; or between about 1 mm and 9 mm; or between about 1 mm and 8 mm; or between about 1 mm and 7 mm; or between about 2 mm and 8 mm; or between about 3 mm and 7 mm; or between about 4 mm and 7 mm; or between about 4 mm and 6 mm; or about 5 mm.

7. (Withdrawn) The method of claim 1, wherein for each electrode, there are at least two said spikes, or at least three said spikes, or at least four said spikes, or at least five said spikes, or at least six said spikes, or at least seven said spikes, or at least eight said spikes, or at least nine said spikes, or at least ten said spikes, or at least twelve said spikes, or at least fifteen said spikes, or at eighteen said spikes, or at least twenty said spikes, or at least twenty-five said spikes, or at least thirty said spikes, or at least thirty-five said spikes, or at least fifty said spikes.

8. (Withdrawn) The method of claim 1 wherein each said spike is up to 250, or up to 240, or up to 230, or up to 220, or up to 210, or up to 200, or up to 190 or up to 180 or up to 170 or up to 160 or up to 150 or up to 140 or up to 130 or up to 120 or up to 110 or up to 100  $\mu\text{m}$  in length.

9. (Withdrawn) The method of claim 1 wherein each said spike is at least 20, or at least 30 or at least 40 or at least 50, or at least 60 or is at least 70 or is at least 80 or is at least 90  $\mu\text{m}$  in length.

10. (Withdrawn) The method of claim 1, wherein each said spike is of sufficient length to penetrate below the skin surface to the *Stratum Germinativum*.

11. (Withdrawn) The method of claim 1, wherein the outer diameter of each spike on the electrodes is between about 20  $\mu\text{m}$  and about 50 $\mu\text{m}$ .

12. (Withdrawn) The method of claim 1, wherein said electrical current has a frequency of between about 10 Hz and about 10 MHz.

13. (Withdrawn) The method of claim 12, wherein step (b) is conducted a first time at a first said frequency, and step (b) is conducted a second time at a second said frequency.

14. (Currently Amended) A method for diagnosing a diseased condition of the skin, the method comprising the steps of:

(i) placing an electrical conducting probe against a skin surface of the subject, wherein the probe comprises a plurality of electrodes, each electrode furnished with a number of spikes, the spikes being laterally spaced apart from each other and being of sufficient length to penetrate the stratum corneum, wherein a first electrode and a second electrode of the plurality of electrodes are spaced a first distance from each other and wherein the first electrode and a third electrode of said plurality of electrodes are spaced a second distance from each other;

(ii) passing an electrical current through the electrodes to obtain a value of skin impedance, wherein said electrical current is separately passed between the first and the second electrode and between the first and the third electrode to obtain at least a first value of impedance and at least a second value of impedance; and

(iii) using reference data to determine whether the impedance value indicates the diseased condition.

15. (Currently Amended) The method of claim 14, wherein the diseased condition is cancer, ~~preferably skin cancer.~~

16. (Currently Amended) The method of claim 15, wherein said ~~skin~~ cancer is a skin cancer selected from the group consisting of basal cell sarcoma, a malignant melanoma, a squamous cell carcinoma, or precursors of such lesions.

17. (Previously Presented) A method according to claim 14, wherein each spike is at least 10  $\mu\text{m}$  in length.

18. (Canceled)

19. (Currently Amended) The method of claim ~~18~~ 14, wherein the first and second distances are different from each other.

20. (Currently Amended) The method of claim ~~18~~ 14, wherein the first distance is between about 0.1 mm and about 40 mm; or between about 0.1 mm and 30 mm; or between about 0.1 mm and 25 mm; or between about 0.1 mm and 20 mm; or between about 0.1 mm and 15 mm; or between about 0.2 mm and 10 mm; or between about 0.2 mm and 8 mm; or between about 0.2 mm and 5 mm; or between about 0.2 mm and 3 mm; or between about 0.2 mm and 2 mm; or between about 0.2 mm and 1.5 mm; or between about 0.2 mm and 1 mm; or between about 0.2 mm and 0.5 mm.

21. (Original) The method of claim 20, wherein the second distance is between about 1 mm and about 50 mm; or between about 1 mm and 40 mm; or between about 1 mm and 30 mm; or between about 1 mm and 25 mm; or between about 1 mm and 20 mm; or between about 1 mm and 15 mm; or between about 1 mm and 10 mm; or between about 1 mm and 9 mm; or between about 1 mm and 8 mm; or between about 1 mm and 7 mm; or between about 2 mm and 8 mm; or between about 3 mm and 7 mm; or between about 4 mm and 7 mm; or between about 4 mm and 6 mm; or about 5 mm.

22. (Previously Presented) The method of claim 14, wherein for each electrode, there are at least two said spikes, or at least three said spikes, or at least four said spikes, or at least five said spikes, or at least six said spikes, or at least seven said spikes, or at least eight said spikes, or at least nine said spikes, or at least ten said spikes, or at least twelve said spikes, or at least fifteen said spikes, or at least eighteen said spikes, or at least twenty said spikes, or at least twenty-five said spikes, or at least thirty said spikes, or at least thirty-five said spikes, or at least fifty said spikes.

23. (Previously Presented) The method of claim 14 wherein each said spike is up to 250, or up to 240, or up to 230, or up to 220, or up to 210, or up to 200, or up to 190 or up to 180 or up to 170 or up to 160 or up to 150 or up to 140 or up to 130 or up to 120 or up to 110 or up to 100  $\mu\text{m}$  in length.

24. (Previously Presented) The method of claim 14 wherein each said spike is at least 20, or at least 30 or at least 40 or at least 50, or at least 60 or is at least 70 or is at least 80 or is at least 90  $\mu\text{m}$  in length.

25. (Currently Amended) The method of claim 14, wherein each said spike is of sufficient length to penetrate below the skin surface to the ~~Stratum Germinativum~~ stratum germinativum or through the ~~Stratum Corneum~~ stratum corneum into the living ~~Epidermis~~ epidermis but not into the ~~Dermis~~ dermis.

26. (Previously Presented) The method of claim 14, wherein the outer diameter of each spike is between about 20  $\mu\text{m}$  and about 50  $\mu\text{m}$ .

27. (Previously Presented) The method of claim 14, wherein said electrical current has a frequency of between about 10 Hz and about 10 MHz.

28. (Currently Amended) The method of claim 27, wherein step-(b) (ii) is conducted a first time at a first said frequency, and step-(b) ii is conducted a second time at a second said frequency.

29. (Previously Presented) The method of claim 14, wherein both non-invasive surface electrodes (conventional probes) are used in conjunction with said minimally invasive spiked electrodes to catch more aspects of skin properties in order to improve power of discrimination.

30. (New) An apparatus for the diagnosing of a diseased condition of the skin of a subject, said apparatus comprising:

an electrically conducting probe including plurality of electrodes, each electrode comprising at least one spike, which spikes are laterally spaced apart from each other and having a length being sufficient to penetrate the stratum corneum, wherein a first electrode and a second electrode of the plurality of electrodes are spaced a first distance from each other and wherein the first electrode and a third electrode of said plurality of electrodes are spaced a second distance from each other,

wherein said apparatus is adapted to, when placed against a skin surface of the subject such that said spikes penetrate the stratum corneum, pass an electrical current through the electrodes to obtain values of skin impedance, wherein said electrical current is separately passed between the first and the second electrode and between the first and the third electrode to obtain at least a first value of impedance and at least a second value of impedance, and to use reference data to determine whether the obtained impedance values indicate the diseased condition.

31. (New) The apparatus according to claim 30, wherein the diseased condition is cancer.

32. (New) The apparatus according to claim 31, wherein said cancer is skin cancer selected from the group consisting of basal cell sarcoma, malignant melanoma, squamous cell carcinoma, or precursors of such lesions.



33. (New) The apparatus according to claim 30, wherein each spike has a length of at least about 10  $\mu\text{m}$ .

34. (New) The apparatus according to claim 30, wherein said first distance and said second distance are different from each other.

35. (New) The apparatus according to claim 30, wherein said first distance is between about 0.1 mm and about 40 mm; or between about 0.1 mm and 30 mm; or between about 0.1 mm and 25 mm; or between about 0.1 mm and 20 mm; or between about 0.1 mm and 15 mm, or between about 0.2 mm and 10 mm; or between about 0.2 mm and 8 mm; or between about 0.2 mm and 5 mm; or between about 0.2 mm and 3 mm; or between about 0.2 mm and 2 mm; or between about 0.2 mm and 1.5 mm; or between about 0.2 mm and 1 mm; or between about 0.2 mm and 0.5 mm.

36. (New) The apparatus according to claim 30, wherein said second distance is between about 1 mm and about 50 mm; or between about 1 mm and 40 mm; or between about 1 mm and 30 mm; or between about 1 mm and 25 mm; or between about 1 mm and 20 mm; or between about 1 mm and 15 mm; or between about 1 mm and 10 mm; or between about 1 mm and 9 mm; or between about 1 mm and 8 mm; or between about 1 mm and 7 mm; or between about 2 mm and 8 mm; or between about 3 mm and 7 mm; or between about 4 mm and 7 mm; or between about 4 mm and 6 mm; or about 5 mm.

37. (New) The apparatus according to claim 30, wherein each electrode comprises at least two said spikes; or at least three said spikes; or at least four said spikes; or at least five said spikes; or at least six said spikes; or at least seven said spikes; or at least eight said spikes; or at least nine said spikes; or at least ten said spikes; or at least twelve said spikes; or at least fifteen said spikes; or at least eighteen said spikes; or at least twenty said spikes; or at least twenty-five said spikes; or at least thirty said spikes; or at least thirty-five said spikes; or at least fifty said spikes.

38. (New) The apparatus according to claim 30, wherein each of said spikes has a length up to about 250  $\mu\text{m}$ , or up to 240  $\mu\text{m}$ , or up to 230  $\mu\text{m}$ , or up to 220  $\mu\text{m}$ , or up to 210  $\mu\text{m}$ , or up to 200  $\mu\text{m}$ , or up to 190  $\mu\text{m}$ , or up to 180  $\mu\text{m}$ , or up to 170  $\mu\text{m}$ , or up to 160  $\mu\text{m}$ , or up to 150  $\mu\text{m}$ , or up to 140  $\mu\text{m}$ , or up to 130  $\mu\text{m}$ , or up to 120  $\mu\text{m}$ , or up to 110  $\mu\text{m}$ , or up to 100  $\mu\text{m}$ .

39. (New) The apparatus according to claim 30, wherein each spike is at least 20; or at least 30; or at least 40; or at least 50; or at least 60; or at least 70; or at least 80, or at least 90  $\mu\text{m}$  in length.

40. (New) The apparatus according to claim 30, wherein each of said spikes has a length being sufficient to penetrate below the skin surface to the stratum germinativum or through the stratum corneum into the living epidermis but not into the dermis.

41. (New) The apparatus according to claim 30, wherein an outer diameter of each of said spikes is between about 20  $\mu\text{m}$  and about 50  $\mu\text{m}$ .
42. (New) The apparatus according to claim 30, wherein said electrical current has a frequency between about 10 Hz and about 10 MHz.
43. (New) The apparatus according to claim 30, wherein said apparatus is adapted to use both non-invasive surface electrodes in conjunction with said spiked electrodes to obtain more aspects of skin properties in order to improve power of discrimination.